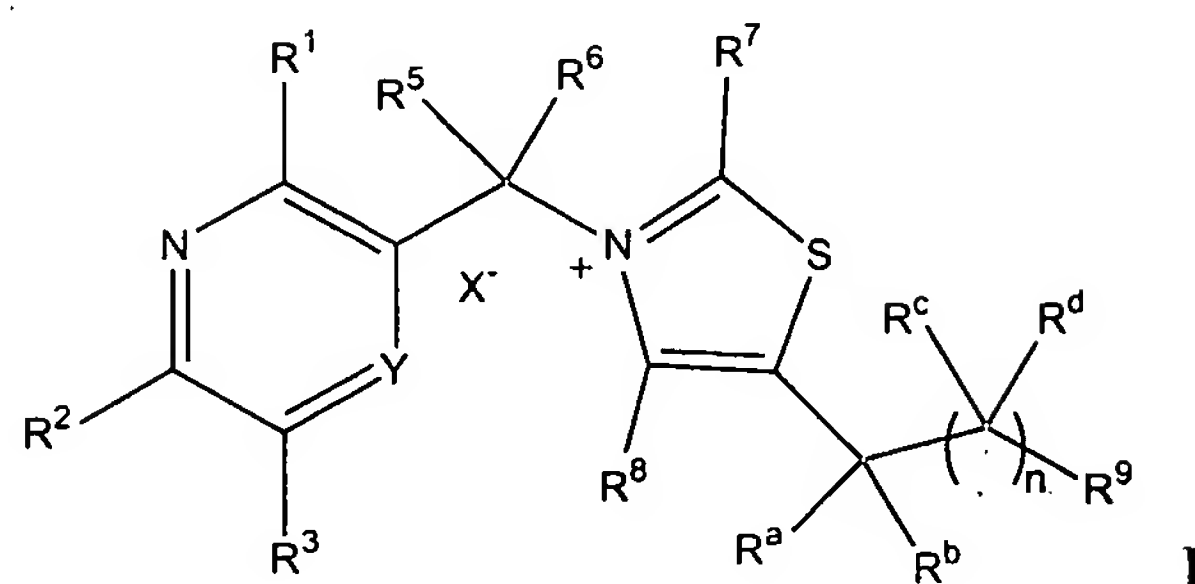


Claim Amendments.

1. (currently amended) A compound of formula I:



or a pharmaceutically acceptable derivative thereof, wherein:

Y is N or C(R<sup>4</sup>);

R<sup>1</sup> is H, alkyl, -N(R)<sub>2</sub>, -(CH<sub>2</sub>)<sub>1-6</sub>N(R<sup>o</sup>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>1-6</sub>OR<sup>o</sup>, -NRC(O)R, -C(O)N(R)<sub>2</sub>, -CN, -NRSO<sub>2</sub>R, -COOR, -OR, -SR, -C(O)R, halo, -OC(O)R, -NRC(O)OR, -OC(O)N(R)<sub>2</sub>, -NRC(O)NR, -NRC(S)NR, -NRSO<sub>2</sub>NR, -C(O)NRN(R)<sub>2</sub>, ~~heteroaryl~~, or ~~heterocyclyl~~;

each R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> is independently H, alkyl, fluoroalkyl, -C(O)R, -COOR, -C(O)N(R)<sub>2</sub>, -CN, -NRC(O)R, -OR, -SR, -N(R)<sub>2</sub>, -(CH<sub>2</sub>)<sub>1-6</sub>OR<sup>o</sup>, -(CH<sub>2</sub>)<sub>1-6</sub>N(R<sup>o</sup>)<sub>2</sub>, or halo;

each R<sup>5</sup> and R<sup>6</sup> is ~~independently H, alkyl, or fluoroalkyl~~;

R<sup>7</sup> is H, alkyl, or fluoroalkyl, ~~aralkyl, carbocyclylalkyl, heterocyclyl, carbocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroaralkyl, C(O)R, (CH<sub>2</sub>)<sub>1-6</sub>OR, (CH<sub>2</sub>)<sub>1-6</sub>N(R)<sub>2</sub>, C(O)CH<sub>2</sub>C(O)R, NRC(O)R, N(R)<sub>2</sub>, C(O)N(R)<sub>2</sub>, or C(H)(OR)R~~;

R<sup>8</sup> is H, alkyl, or fluoroalkyl, ~~carbocyclyl, carbocyclylalkyl, heteroaryl, heterocyclyl, CO<sub>2</sub>R, or CON(R)<sub>2</sub>~~;

R<sup>9</sup> is -OR<sup>10</sup> or -NR<sup>11</sup>R<sup>12</sup>;

R<sup>10</sup> is R<sup>o</sup>, -C(O)R, -C(O)N(R)<sub>2</sub>, -C(O)OR, -(CH<sub>2</sub>)<sub>1-6</sub>-C(O)R, -PO<sub>3</sub>M<sub>x</sub>, -P(O)(alkyl)OM', or -(PO<sub>3</sub>)<sub>2</sub>M<sub>y</sub>, ~~carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor targeting moiety~~;

x is 1 or 2;

y is 1, 2 or 3;

each M is independently H, Li, Na, K, Mg, Ca, Mn, Co, Ni, Zn, or alkyl;

M' is H, Li, Na, K, or alkyl;

R<sup>11</sup> is H or alkyl;

R<sup>12</sup> is H, alkyl, -C(O)R, -C(O)N(R)<sub>2</sub>, -C(O)OR, -SO<sub>2</sub>R, or -SO<sub>2</sub>N(R)<sub>2</sub>,  
~~carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl,~~  
~~heteroaralkyl or a tumor targeting moiety;~~

each R<sup>a</sup> and R<sup>b</sup> is independently H, ~~OR<sup>o</sup>~~, alkyl, or fluoroalkyl -OH;

each R<sup>c</sup> and R<sup>d</sup> is ~~independently H, alkyl, or fluoroalkyl;~~

n is 0-4;

X<sup>-</sup> is a monovalent or divalent anion, or a counterion to the thiazolium nitrogen  
located anywhere in the molecule;

R<sup>o</sup> is H or alkyl; and

R is R<sup>o</sup>, ~~carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl,~~  
~~heterocyclylalkyl, or heteroaralkyl;~~

provided that the following compounds are excluded:

Y is C(R<sup>4</sup>);

R<sup>5</sup>, R<sup>6</sup>, R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup> and R<sup>d</sup> are H;

R<sup>8</sup> is methyl;

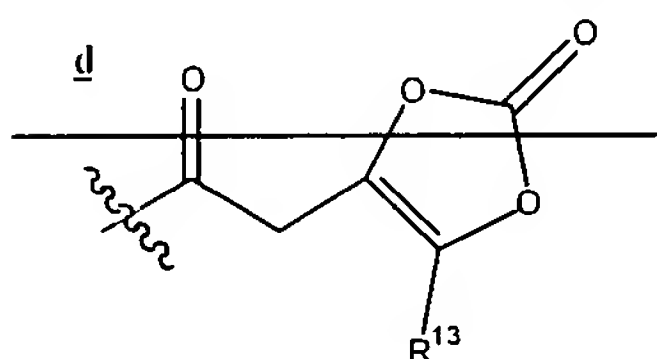
R<sup>9</sup> is -OR<sup>10</sup>, and R<sup>10</sup> is H, -PO<sub>3</sub>M<sub>x</sub>, -(PO<sub>3</sub>)<sub>2</sub>M<sub>y</sub> or -P(O)(alkyl)OM';

X<sup>-</sup> is Cl<sup>-</sup> or Br<sup>-</sup>;

- i) R<sup>1</sup> is H, R<sup>2</sup> is methyl, R<sup>3</sup> is -OH, R<sup>4</sup> is methyl, -CH<sub>2</sub>OH or  
-CH<sub>2</sub>NH<sub>2</sub>, and R<sup>7</sup> is H;
- ii) R<sup>1</sup> is -NH<sub>2</sub>, -NHMe or -N(Me)<sub>2</sub>, R<sup>2</sup> is methyl, R<sup>3</sup> is H, R<sup>4</sup> is H or -CH<sub>3</sub>,  
and R<sup>7</sup> is H;
- iii) R<sup>1</sup> is -NH<sub>2</sub> or OH, R<sup>2</sup> is methyl, R<sup>3</sup> is H, R<sup>4</sup> is H, and R<sup>7</sup> is H;
- iv) R<sup>1</sup> and R<sup>3</sup> are H, R<sup>2</sup> is methyl, R<sup>4</sup> is -NH<sub>2</sub>, and R<sup>7</sup> is H;
- v) R<sup>1</sup> is -NH<sub>2</sub>, R<sup>2</sup> is methyl, R<sup>3</sup> and R<sup>4</sup> are H, and R<sup>7</sup> is H,  
-CH(OH)CO<sub>2</sub>H or -C(OH)(Me)CO<sub>2</sub>H;
- vi) R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>7</sup> are H and R<sup>2</sup> is methyl; and
- vii) R<sup>1</sup> is H, R<sup>2</sup> is -NH<sub>2</sub>, R<sup>3</sup> is -OH, R<sub>4</sub> is -CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, and R<sup>7</sup> is H.

2. (currently amended) The compound of claim 1, wherein  $R^{10}$  is  $R^o$ ,  $-C(O)R$ ,  $-C(O)N(R)_2$ ,  $-C(O)OR$ ,  $-(CH_2)_{1-6}-C(O)R$ , or alkyl, ~~carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety~~; and  $R^{12}$  is  $-C(O)R$ ,  $-C(O)N(R)_2$ ,  $-C(O)OR$ ,  $-SO_2R$ , or  $-SO_2N(R)_2$ , ~~carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor-targeting moiety~~.

3. (currently amended) The compound of claim 1, wherein  $R^{10}$  is  $R^o$  ~~or~~ and  $R^{12}$  is a polysaccharide,  $-[C(O)CH(R)N(R)]_{2-3}-R$ , ~~an antibody, or~~



~~, wherein  $R^{13}$  is H, alkyl, or aryl.~~

4. (cancelled).

5. (currently amended) The compound of claim 4 1, wherein:

i)  $R^1$  is  $\underline{N(R)_2}$ ,  $-(CH_2)_{1-6}N(R^\circ)_2$ ,  $-(CH_2)_{1-6}OR^\circ$ ,  $-NRC(O)R$ ,  $-C(O)N(R)_2$ ,  $-CN$ ,  $-N(R)SO_2R$ ,  $-COOR$ ,  $-SR$ ,  $-C(O)R$ , halo,  $-OC(O)R$ ,  $-NRC(O)OR$ ,  $-OC(O)N(R)_2$ ,  $-N(R)C(O)N(R)$ ,  $-NRC(S)NR$ ,  $-NRSO_2NR$ , or  $-C(O)NRN(R)_2$ , ~~heteroaryl, or heterocyclyl;~~

ii)  $R^2$  is H, alkyl, fluoroalkyl,  $-C(O)R$ ,  $-COOR$ ,  $-C(O)N(R)_2$ ,  $-CN$ ,  $-NRC(O)R$ ,  $-OR$ ,  $-SR$ ,  $-N(R)_2$ ,  $-(CH_2)_{1-6}OR^\circ$ ,  $-(CH_2)_{1-6}N(R^\circ)_2$ , or halo;

iii)  $R^3$  is H, alkyl, fluoroalkyl,  $-C(O)R$ ,  $-COOR$ ,  $-C(O)N(R)_2$ ,  $-CN$ ,  $-NRC(O)R$ ,  $-SR$ ,  $-N(R)_2$ ,  $-(CH_2)_{1-6}OR^\circ$ ,  $-(CH_2)_{1-6}N(R^\circ)_2$ , or halo;

iv)  $R^4$  is H, fluoroalkyl,  $-C(O)R$ ,  $-COOR$ ,  $-C(O)N(R)_2$ ,  $-CN$ ,  $-NRC(O)R$ ,  $-OR$ ,  $-SR$ ,  $-(CH_2)_{1-6}N(R^\circ)_2$ , or halo;

v)  $R^{10}$  is H,  $-PO_3M_x$ ,  $-(PO_3)_2M_y$  or  $-P(O)(alkyl)OM'$ ; or  $R^{12}$  is H or  $C_{1-6}$  alkyl;  
and

vi)  $n$  is 1.

6. (cancelled).

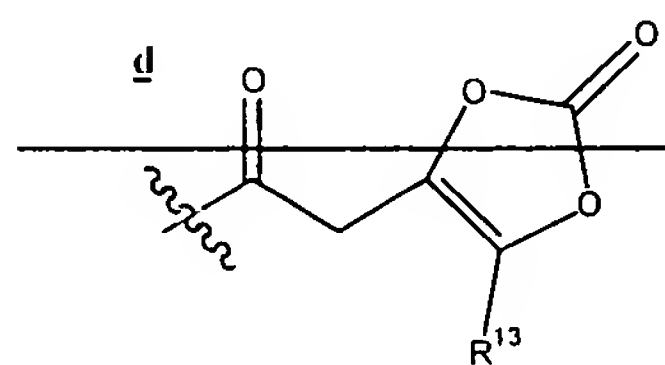
7. (currently amended) The compound of ~~6~~ 1, wherein:

- i)  $R^1$  is H,  $-N(R)_2$ , alkyl,  $-NR^oC(O)NR$ ,  $-NR^oC(O)OR$ ,  $-C(O)N(R)_2$ ,  $-(CH_2)_{1-6}N(R^o)_2$ ,  $-NR^oC(O)R$ ,  $-CN$ ,  $-COOR$ ,  $-OR$ ,  $-SR$ , or halo;
- ii)  $R^2$  is H, alkyl, fluoroalkyl,  $-OR^o$ ,  $-N(R^o)_2$ , or halo;
- iii)  $R^3$  and  $R^4$  are independently H, alkyl,  $-OR$ ,  $-N(R)_2$ ,  $-(CH_2)_{1-6}OR^o$ , or  $-(CH_2)_{1-6}N(R^o)_2$ ;
- iv)  $R^7$  is H, alkyl, or fluoroalkyl,  ~~$-(CH_2)_{1-6}OR$ ,  $-(CH_2)_{1-6}N(R)_2$ ,  $-NR^oC(O)R$ ,  $-C(O)R$ ,  $-C(H)(OR)R$ , aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl;~~
- v)  $R^{10}$  is H, alkyl,  $-C(O)R$ ,  $-PO_3M_x$ ,  $-P(O)(alkyl)OM'$ ,  $-(PO_3)_2M_y$ ,  $-C(O)N(R)_2$ , or  $-C(O)OR$ , ~~or a tumor-targeting moiety; or~~ and  $R^{12}$  is H, alkyl,  $-C(O)R$ ,  $-C(O)N(R)_2$ ,  $-C(O)OR$ , or  $-SO_2R$ , ~~5-membered heterocyclyl, 5-membered heteroaralkyl, or a tumor-targeting moiety;~~ and
- vi)  $n$  is 1.

8. (cancelled).

9. (currently amended) The compound of claim ~~8~~ 1, wherein  $R^o$  is H or  $C_{1-6}$  alkyl optionally substituted with halo, hydroxy or amino.

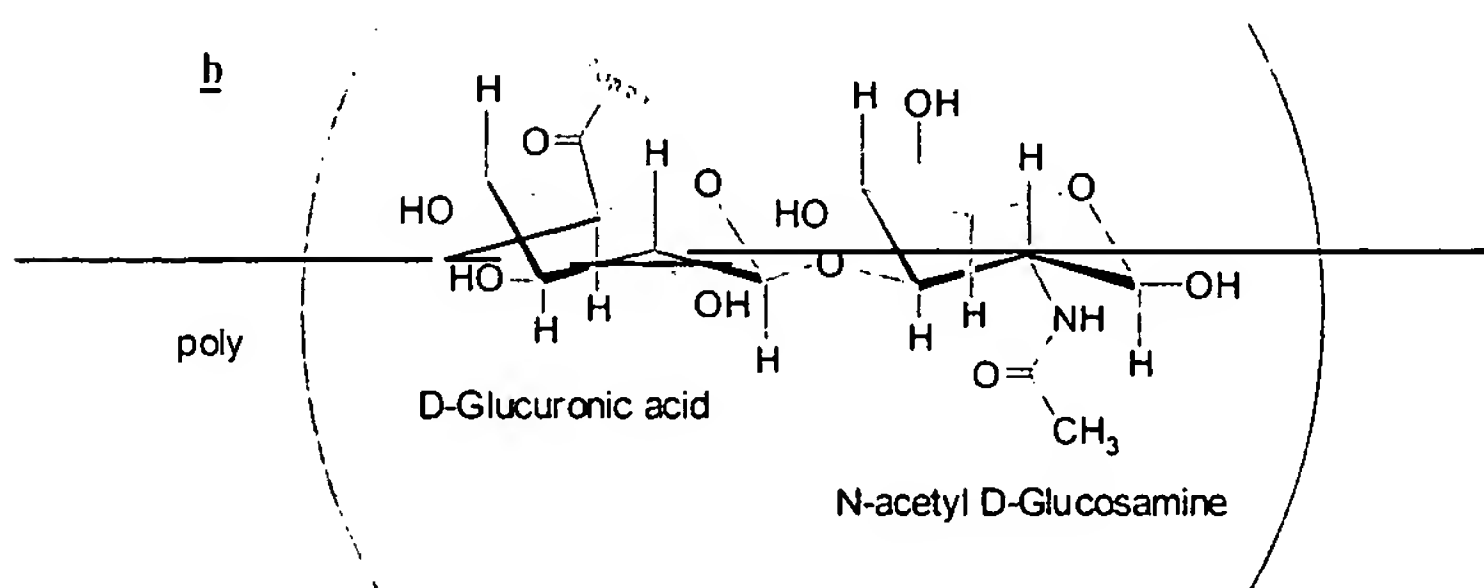
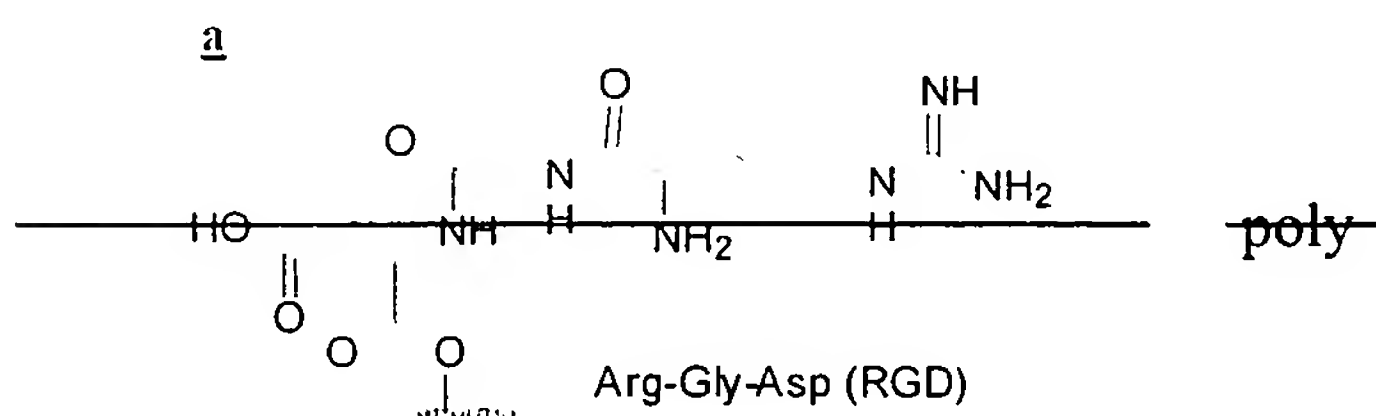
10. (currently amended) The compound of claim ~~6~~ or 7, wherein  $R^{10}$  is  $R^o$  and ~~or~~  $R^{12}$  is a polysaccharide,  $-[C(O)CH(R)N(R)]_{2-3}-R$ , ~~an antibody, or~~



~~, wherein  $R^{13}$  is H, alkyl, or aryl.~~

11. (currently amended) The compound of claim 6 or 7, wherein ~~said compound has one or more of the features selected from the group consisting of:~~

- i)  $R^1$  is H, amino,  $-\text{CH}_2\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NHEt}$ ,  $-\text{NHC}(\text{O})\text{OEt}$ ,  $-\text{NHCH}_2\text{OH}$ ,  $-\text{NHCH}_2\text{CH}_2\text{OH}$ ,  $-\text{NH}-\text{CH}_2\text{CH}_2\text{Cl}$ ,  $-\text{N}(\text{CH}_2\text{OH})_2$ , Cl, Br,  $-\text{SCH}_3$ , CN,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{OH}$ , methyl, or ethyl;
- ii)  $R^2$  is H, methyl, ethyl, amino,  $\text{CF}_3$ , Cl, or Br;
- iii)  $R^3$  is H, methyl, ethyl, amino, or hydroxy;
- iv)  $R^4$  is H, methyl, ethyl,  $-\text{CH}_2\text{OH}$ , or  $-\text{CH}_2\text{NH}_2$ ;
- v) ~~each  $R^5$ ,  $R^6$  and  $R^8$  is independently~~ H, methyl, ethyl,  $-\text{CH}_2\text{F}$ ,  $-\text{CHF}_2$ , or  $-\text{CF}_3$ ;
- vi)  $R^7$  is H, methyl, ethyl, or  $\text{CF}_3$ ,  ~~$-\text{CH}(\text{OH})\text{CH}_3$ ,  $-\text{CH}_2\text{OH}$ , or  $-\text{CH}_2\text{CH}_2\text{OH}$~~ ; and
- vii)  $R^{10}$  is H, methyl, ethyl,  $-\text{C}(\text{O})\text{Me}$ ,  $-\text{C}(\text{O})\text{Et}$ ,  $-\text{C}(\text{O})\text{NMe}_2$ ,  ~~$-\text{C}(\text{O})$ -p-OMe-phenyl,  $-\text{C}(\text{O})$ -O-phenyl,  $-\text{PO}_3\text{H}_2$ ,  $-\text{P}(\text{O})(\text{OMe})_2$ ,  $-\text{P}(\text{O})(\text{OMe})\text{OH}$ ,  $-\text{P}(\text{O})(\text{Me})\text{OH}$ ,  $-\text{P}(\text{O})(\text{OH})\text{OP}(\text{O})(\text{OH})(\text{OH})$ , or  $R^{14}$~~ ; and  ~~$R^{14}$  is selected from the group consisting of:~~

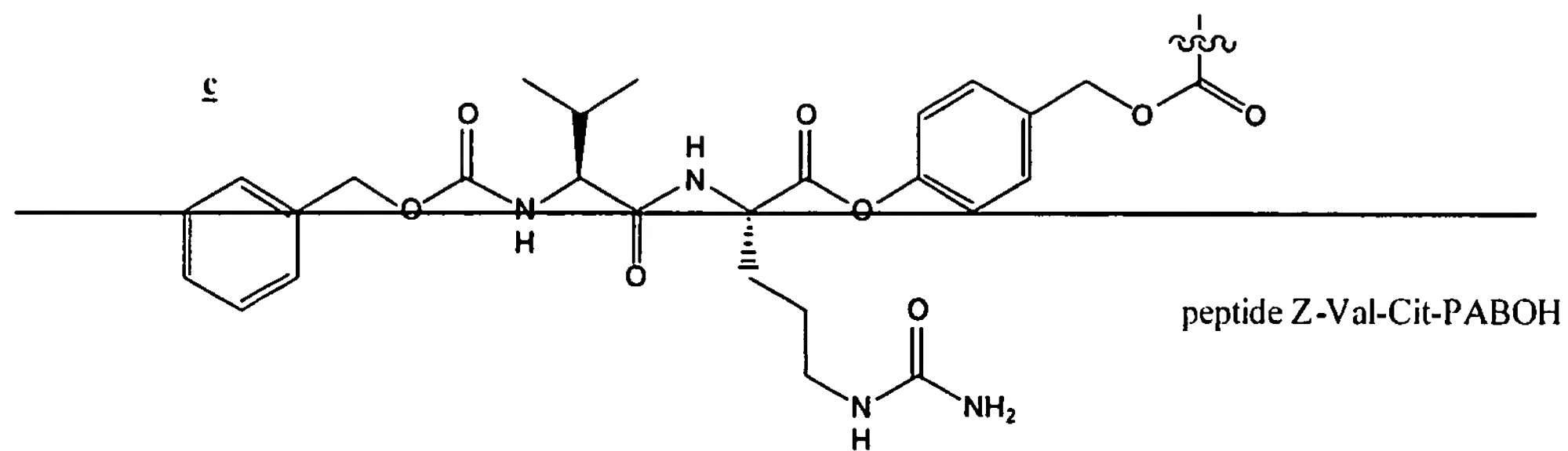


A33-012

Serial No. 10/593,910

Response to November 20, 2009 Office Action

Page 8 of 17



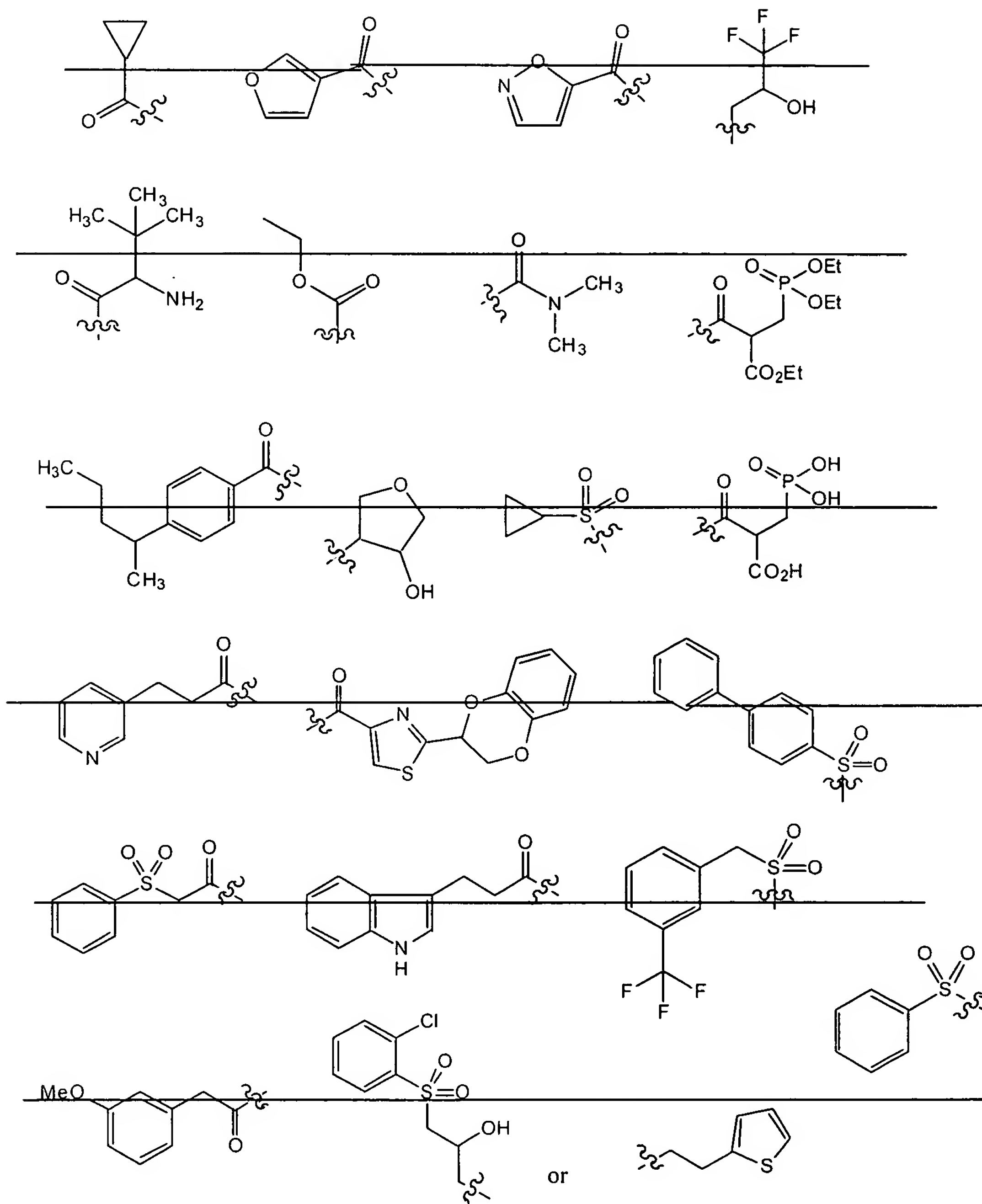
antibody; or and  $R^{12}$  is H, methyl, or ethyl,  $R^{14}$ ;

A33-012

Serial No. 10/593,910

Response to November 20, 2009 Office Action

Page 9 of 17

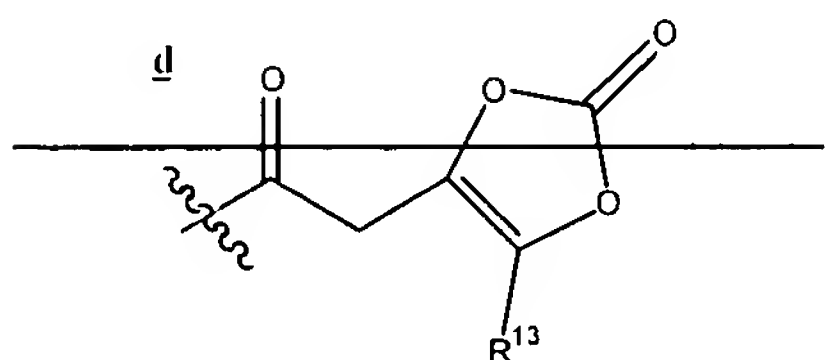




12. (currently amended) The compound of claim 6 or 7, wherein ~~said compound has one or more of the features selected from the group consisting of:~~

- i)  $R^1$  is H,  $-N(R^0)_2$ ,  $-SR^0$ , or halo;
- ii)  $R^2$  is H, alkyl, fluoroalkyl,  $-N(R^0)_2$ , or halo;
- iii)  $R^3$  and  $R^4$  are independently H or alkyl;
- iv)  $R^7$  is H or alkyl;
- v)  $R^8$  is H or  $C_{1-6}$  unsubstituted alkyl; and
- vi)  $R^9$  is  $-OR^{10}$  and  $R^{10}$  is H,  $C_{1-6}$  unsubstituted alkyl,  $-C(O)R$ ,  $-PO_3M_x$ ,  $-P(O)(alkyl)OM'$ ,  $-(PO_3)_2M_y$ , or  $-C(O)OR$ , ~~or a tumor targeting moiety.~~

13. (currently amended) The compound of claim 12, wherein  $R^{10}$  is ~~a polysaccharide,  $-[C(O)CH(R)N(R)]_{2-3}-R$ , an antibody, or~~ H,  $C_{1-6}$  unsubstituted alkyl, or  $-C(O)R$



wherein  $R^{13}$  is ~~H, alkyl, or aryl.~~

14. (currently amended) The compound of claim 12, wherein ~~said compound has one or more of the features selected from the group consisting of:~~

- i)  $R^1$  is H,  $-NH_2$ ,  $-SCH_3$ , or Cl;
- ii)  $R^2$  is H, methyl, ethyl,  $-CF_3$ ,  $-NH_2$ , or Cl;
- iii)  $R^3$ ,  $R^4$ ,  $R^7$  and  $R^8$  are independently H or, methyl, or ethyl; and
- iv)  $R^9$  is  $-OR^{10}$  and  $R^{10}$  is ~~H, H,  $-R^0$ ,  $PO_3H_2$ ,  $-P(O)(OMe)_2$ ,  $-P(O)(OMe)OH$ ,  $-P(O)(Me)OH$ , or  $-P(O)(OH)OP(O)(OH)(OH)$ , or  $R^{14}$ ; and  $R^{14}$  is as defined in 11.~~

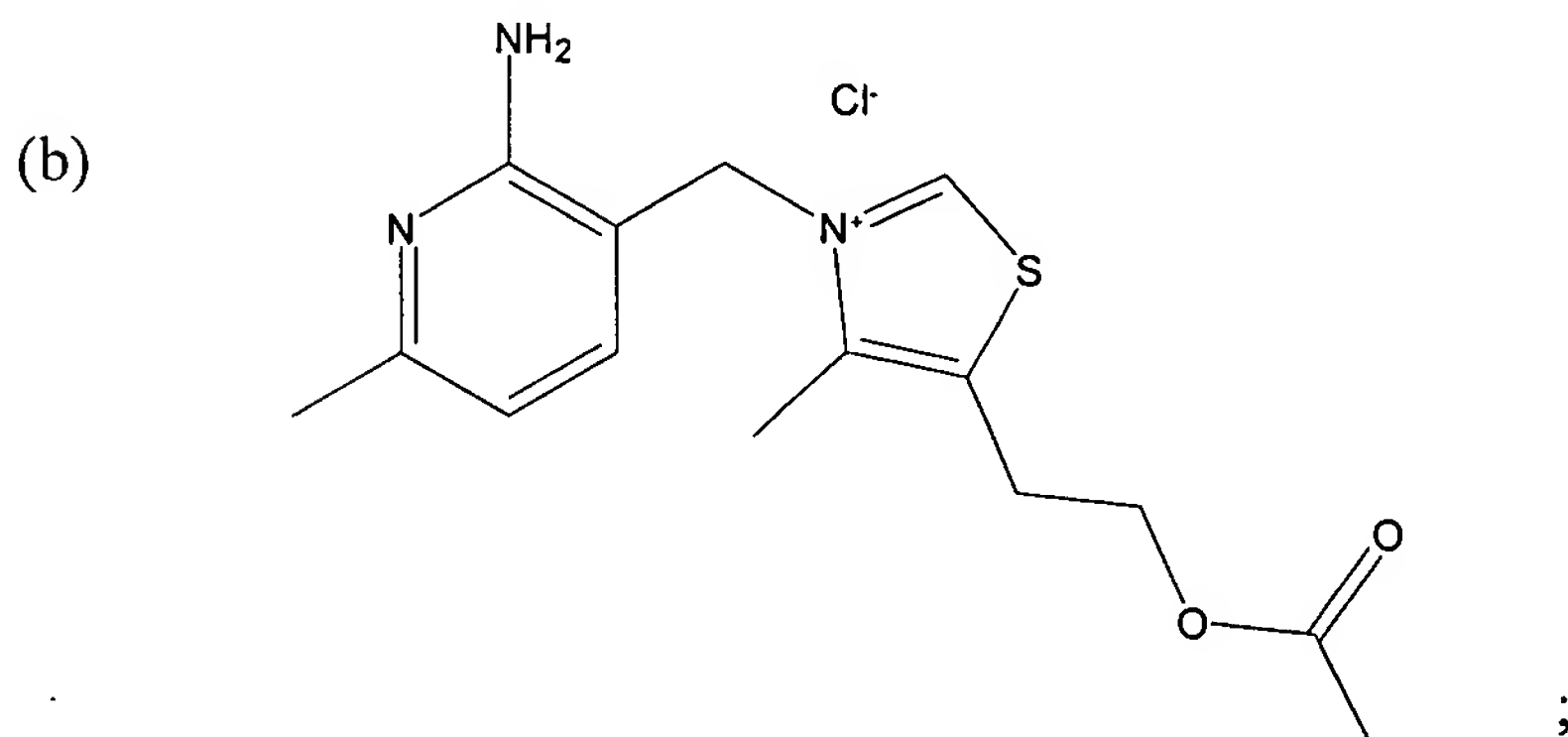
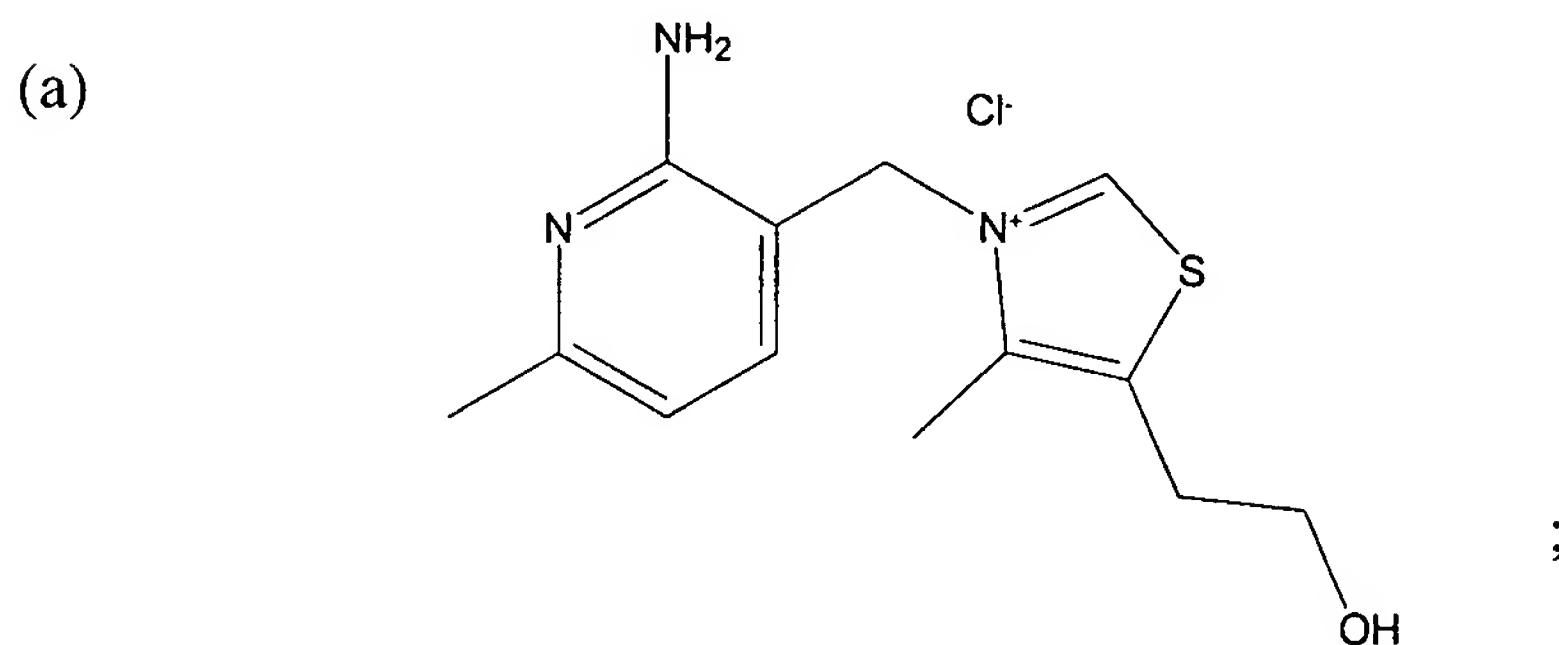
15. (previously amended) The compound of claim 1, wherein said compound is IIa-1, IIa-2, IIa-3, IIa-4, IIa-5, IIa-6, IIa-7, IIa-8, IIa-9, IIa-10, IIa-11, or IIc-1.

16. (currently amended) A pharmaceutical composition comprising a compound of ~~claim 1~~  
claims 1-15 and a pharmaceutically acceptable carrier.

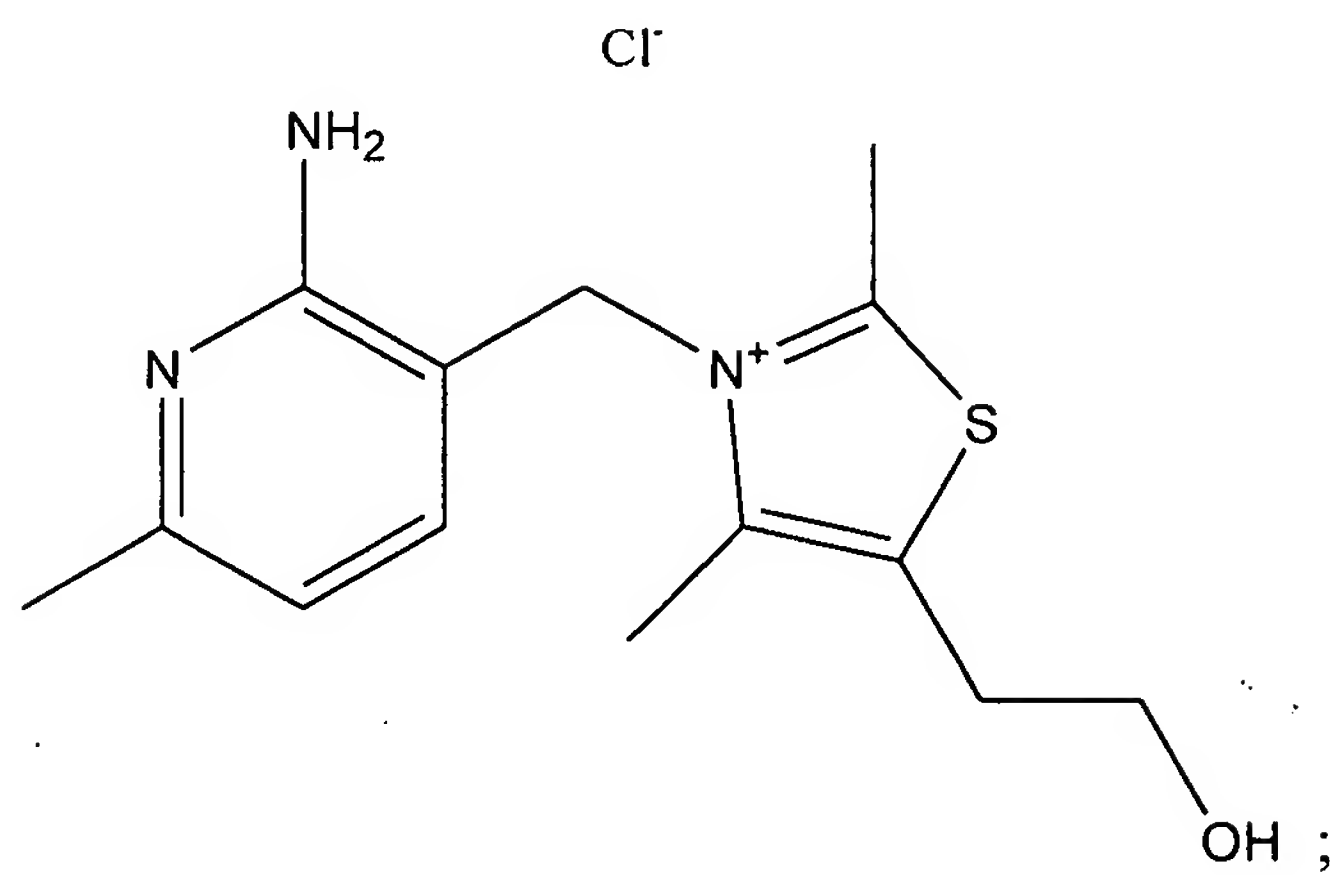
17. (previously amended) The composition of claim 16, further comprising at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

18.-27. (cancelled).

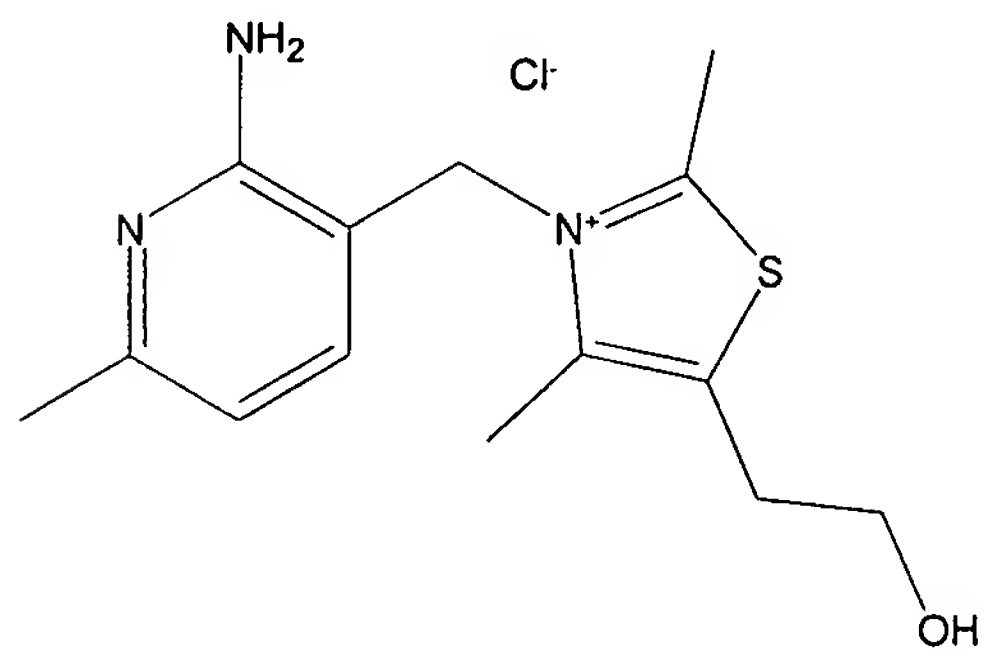
28. (new) The compound of formula 1, wherein the compound is selected from the group consisting of:



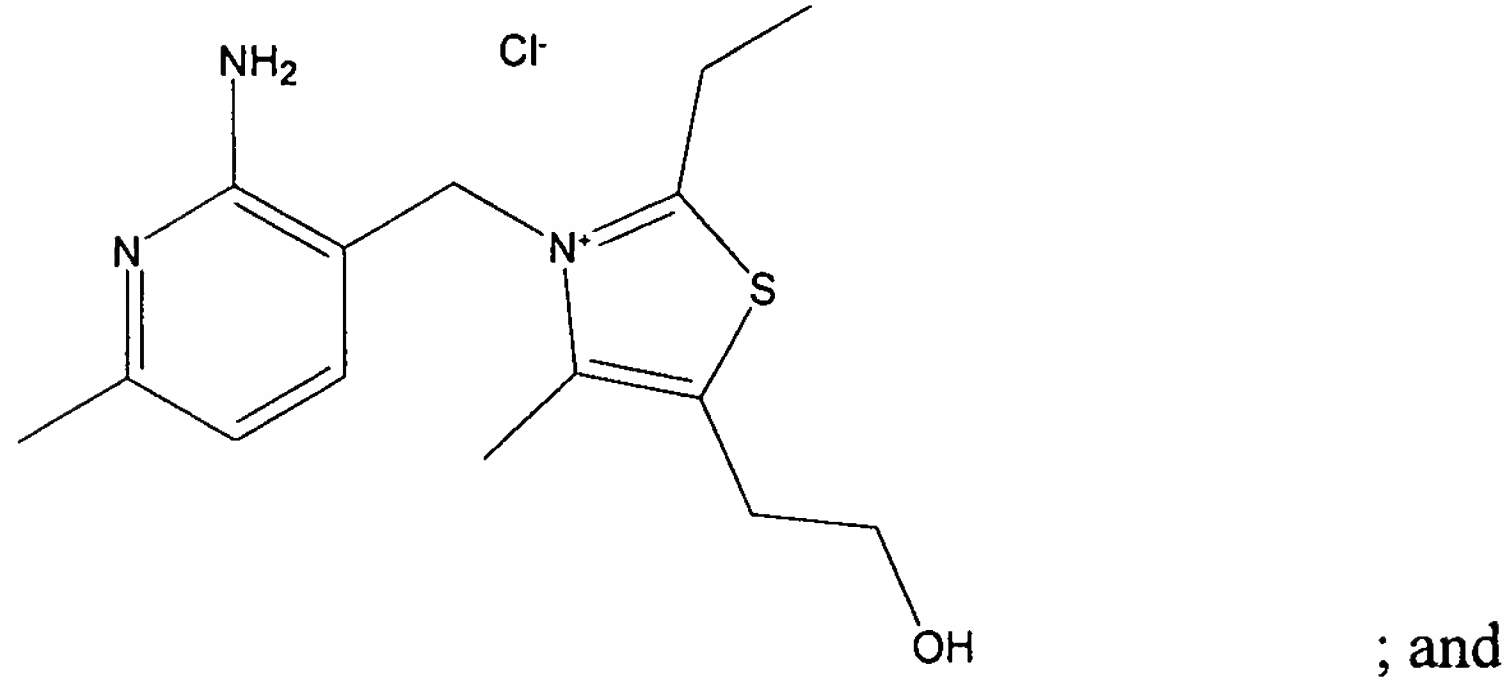
(c)



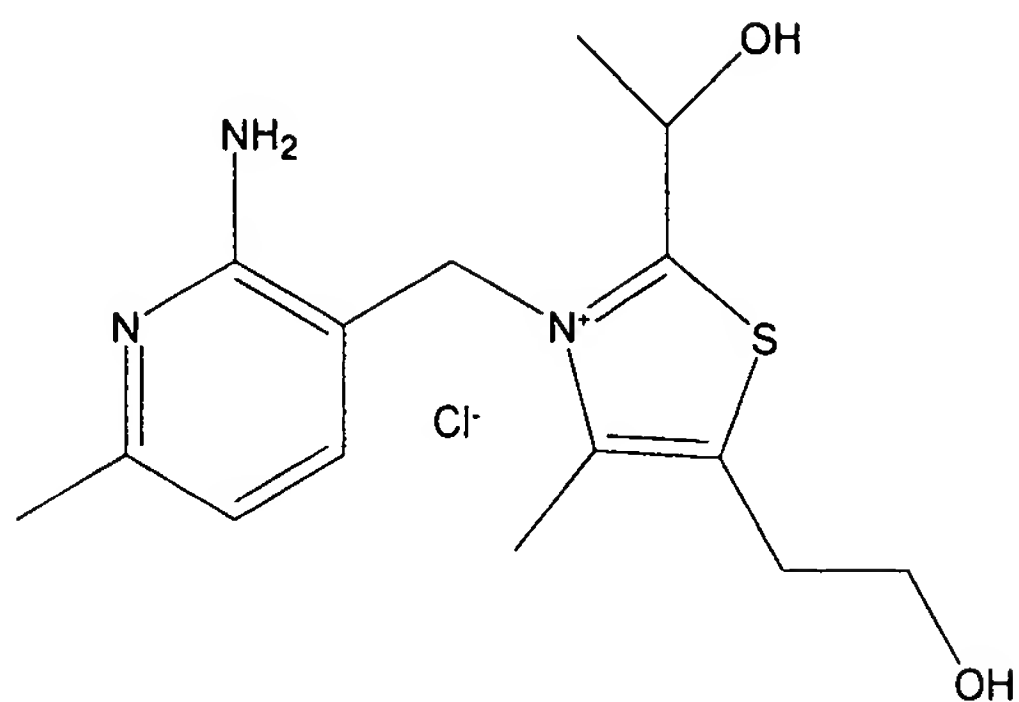
(d)



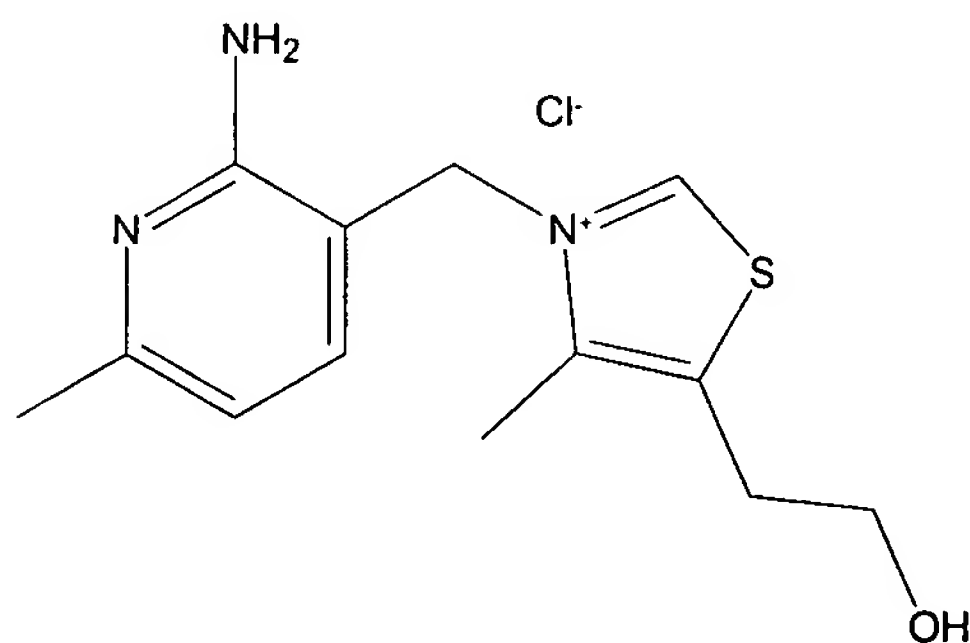
(e)



(f)



29. (new) The compound of formula 1, wherein the compound is



30. (new) The compound of claim 1, wherein:

$\text{R}^1$  is H or  $-\text{N}(\text{R})_2$ ;

$\text{R}^2$  is H or alkyl;

$\text{R}^3$  and  $\text{R}^4$  are independently H or alkyl;

$\text{R}^7$  is H or alkyl;

$\text{R}^8$  is H or  $\text{C}_{1-6}$  unsubstituted alkyl;

$\text{R}^9$  is  $-\text{OR}^{10}$  and  $\text{R}^{10}$  is H,  $\text{C}_{1-6}$  unsubstituted alkyl, or  $-\text{C}(\text{O})\text{R}$ ;

$\text{R}^a$ ,  $\text{R}^b$ ,  $\text{R}^c$ , and  $\text{R}^d$  are H; and

$n$  is 1.